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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,998	04/07/2004	Randolph A. Moeckli	544042000100	9298

25226 7590 12/05/2005

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EXAMINER	
ROOKE, AGNES BEATA	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

[redacted]

Office Action Summary	Application No.	Applicant(s)	
	10/820,998	MOECKLI ET AL.	
	Examiner	Art Unit	
	Agnes B. Rooke	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *39-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,15-17,19-32,37 and 38* is/are rejected.

7)☒ Claim(s) *13,14,18 and 33-36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *Nov 8, 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, claims 1-38 in the reply filed on 09/16/2005 is acknowledged.

Therefore, the restriction requirement is deemed proper and is made FINAL.

Claims 1-38 are pending and currently under examination. Claims 39-66 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, and further, withdrawn claims should be properly labeled as "withdrawn."

A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP paragraph 821.01.

This application claims priority to 60/462,483, filed on 04/10/2003.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 15-17, 21, 25, 28, 30-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claims 15, 17, 21, 25, 28, and 30-32, the structures of all possible fragments of the claimed proteins or their analogs are not adequately described in the specification, and thus the structures do not correspond with their function.

The following factors are considered to assess if Applicants were in possession of the invention:

a. Actual reduction to practice: Applicants did not reduce to practice all possible fragments or analogs of the claimed proteins that are capable of binding cognate ligand.

b. Disclosure of structural chemical formulas: the structure of all possible fragments or analogs of the claimed proteins that are capable of binding the cognate ligand are not disclosed.

c. Sufficient relevant identifying characteristics: the full structure of the claimed proteins is provided but the structures for all possible analogs that are capable of binding the cognate ligand are not disclosed.

d. Method of making the claimed invention: all possible analogs that are capable of binding the cognate ligand are not properly disclosed for making of the invention.

e. Level of skill and knowledge in the art: the level of skill is would be somebody with a PhD in the art.

f. Predictability of the art: it is not predictable which fragments and analogs might be capable of binding to the cognate ligand since the specification does not discuss which portion of the troponin molecule is responsible for the binding the cognate ligand.

Claims 1, 15-17, 21, 25, 28, 30-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable a person skilled in the art to which it pertains, or with which it is mostly connected, to make or use the invention commensurate in scope with these claims. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are: 1) the nature of the invention, 2) the breadth of the claims, 3) the state of the prior art, 4) the predictability or lack thereof in the art, 5) the amount of direction or guidance present, 6) the presence or absence of working examples, 7) the quantity of experimentation needed, and 8) the level of the skill in the art.

1) The nature of the invention: the invention is a method for purifying a troponin-tagged molecule where different fragments or analogs are used;

2) the breadth of the claims: the claims are broad because there could be an infinite number of different fragments of the polypeptides or analogs that are used in the method;

3) the state of the prior art: the full sequence of the polypeptides are disclosed by applicants;

4) the predictability or unpredictability of the art: there could be an infinite amount of the fragments and analogs of the claimed polypeptides and thus the art is unpredictable; it is unpredictable which fragments and analogs will be capable of binding the cognate ligand and there will be different dependency on which ligand is selected;

5) the amount of direction or guidance present: the full sequence of the polypeptides are disclosed, however there is no guidance as to which specific fragments or analogs of these polypeptides would be capable of binding the cognate ligand;

6) the presence or absence of working examples: there are no working examples that would cover all possible fragments and analogs of the claimed polypeptides that would be capable of binding the cognate ligand;

7) the quantity of experimentation necessary: there would be a large amount of experimentation necessary to determine, and characterize all possible fragments and analogs of the claimed polypeptides claimed because there are so many possibilities;

8) the relative skill of those skilled in the art: a person skilled in the art would have a PhD in the art.

In consideration of the *In re Wands* factors 1-8, it is apparent that there is undue experimentation necessary because of variability in prediction of the outcome that is not addressed by the present application disclosure, example, and teachings. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

[redacted]

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12, 15, 16, 19, 20-29, 31, 37, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al. in view of Ault-Riche et al.

Neri et al. teach that the prior art discloses a fusion of calmodulin binding ligand tag derived from the C terminus of rabbit skeletal muscle myosin light chain kinase and a recombinant protein, where the fusion protein was used in purification strategies on an affinity support; where in the presence of high level of calcium the system displays a specific high affinity interaction; where the addition of EGTA lowers the affinity of the interaction. See column 1, lines 62-67; column 2, lines 1-10.

Further, Neri et al. state that the present invention provides a ligand capable of binding a calcium dependent binding protein comprising an amino acid sequence corresponding to that of a wild type ligand for the calcium dependent binding protein, with a modification which results in enhanced affinity of the ligand for the calcium dependent binding protein. See column 2, lines 28-35.

The preferred calcium dependent binding protein is calmodulin; where hybrid recombinant proteins of calmodulin and another protein may be easily generated by genetic fusions; where the use of a small protein as a tag reduces the risk of perturbing the protein structure of the fusion partner. See column 3, lines 59-67.

[redacted]

In column 4, line 5, Neri et al. state that it will be understood that other calcium-dependent binding proteins such as troponin C may also be employed in the present invention.

In column 4, lines 18-21, Neri et al. state that it is preferred that the ligand of the present invention shows a reduction in Kd by a factor of at least 10, preferably by a factor of at least 100.

In column 5, lines 6-33, Neri et al. state that in the invention provides use of a ligand according to the present invention in conjunction with a calcium dependent binding protein as a binding pair; where the calmodulin can be linked to an enzyme, for example; See column 5, lines 45-46 where the linked moiety maybe a protein; in column 5, lines 57-62, Neri et al. state that the linked moiety may be appended to the ligand non-covalently, or by chemical modification by linking reactive functional groups such as amino or carboxy, for example.

In claims 17 and 19, Neri et al. claim a method for binding two molecules, which method comprises contacting a molecule comprising a calcium dependent binding protein with a molecule comprising a modified ligand under conditions that permit binding of the calcium dependent binding protein and the modified ligand (claim 17); and the method wherein the molecules are immobilized (claim 19).

Neri et al. does not disclose different type of matrices for immobilization of proteins.

Ault-Riche et al. disclose in [0060] commonly used matrix support systems, which is any solid or semisolid or insoluble support or solid support, to which a molecule

of interest, typically a biological molecule is linked or contacted; where such materials include any material that are used as affinity matrices like agarose, polysaccharides, or glass, for example.

Claims 21-27 are included in this rejection because the applicant claims that affinity matrix comprises troponin I, or a fragment or analogue thereof that is capable of binding troponin C. A fragment of a polypeptide could be even a single amino acid, a series of unidentified amino acids. Therefore, Neri et al. would be a prior art for claims 21-27, because Neri et al. teach in claim 17 and 19, a method for binding two molecules, which method comprises contacting a molecule comprising a calcium dependent binding protein with a molecule comprising a modified ligand under conditions that permit binding of the calcium dependent binding protein and the modified ligand (claim 17); and the method wherein the molecules are immobilized (claim 19).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to design a method of purifying a troponin-tagged molecule where the troponin-tagged molecule is contacted with an affinity matrix, such as glass or agarose as taught by Ault-Riche et al., that comprises a cognate ligand, and where the troponin tagged molecule is immobilized on the affinity matrix as taught by Neri et al.

One would be motivated to improve upon the Neri et al. in view of Ault-Riche et al. because troponin C can be used instead of calmodulin since Neri at al. state that

their invention relates to targeting, detection, immobilization, and purification of molecules using binding pairs and that the binding pairs of the present invention provide an attractive alternative to currently available binding pair systems.

Objections to claims

Claims 13, 14, 18, 33, 34, 35, and 36 stand objected because they depend from rejected base claim.

Prior art of record:

1.SEQ ID NO:4 is known in the prior art and was published in Nature 418:79-85 (2002) "Sequence and analysis of chromosome 2 of Dictyostelium discoideum."

2. Neri et al. U.S. 6,495,673 B1, claims 1-16, which refer to a method of isolating DNA encoding an enzyme, where the enzyme is isolated by binding the product of a solid matrix.

3. Shi et al. U.S. 2002/0127,602 A1, in [0001] the invention relates to new polypeptides corresponding to human cardiac troponin I N-terminal fragments and their uses as immunogens, affinity reagents, and standards for the preparation and calibration of improved immunoassays for troponin I; where troponin I is an isoform of troponin C [0003].

Conclusion

No claims are allowed.

[redacted]

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

AR

ROBERT A. WAX
PRIMARY EXAMINER